information requested by the examiner regarding the relationship of the present application to the PCT application. Additionally, as requested by the examiner, page 3 is amended to recite the date of deposit and the complete name and full address of the depository. No new matter has been added.

1. Specification

Applicants have amended the specification to recite the priority documents in the manner requested by the examiner. It is believed this amendment removes the examiner's objection to the specification.

2. Information Disclosure Statement

As requested by the examiner, a PTO 1449 is attached that cites the 1997 publication attached as Appendix A in the response filed on October 13, 1998 so that this publication appears on the face of the issued patent.

3. Claim Objections

The typographical errors noted by the examiner in claims 25 and 28 are corrected and claim 18 is cancelled.

4. Rejection under 35 U.S.C. § 112, second paragraph

Claims 15 - 28 are rejected as indefinite for reciting in claim 15 "administering a therapeutically effective amount of an antibody to an IL-6 receptor" because the claim allegedly does not provide a functional limitation for the effective amount. Applicants have amended claim 15 to recite functionally the therapeutic effective amount administered.

5. Rejections under 35 U.S.C. § 112, first paragraph

Claims 25 and 28 are rejected as allegedly not being enabled because the examiner did not find sufficient the deposit receipt showing that the PM-1 hybridoma producing the PM-1 monoclonal antibody was deposited on July 10, 1990 as deposit accession number FERM BP-2998 at the National Institute of Bioscience and Human-Technology, a Budapest recognized depository to overcome this rejection.

Applicants herewith attach a Declaration under 35 U.S.C. § 1.132 by one of the inventors, Dr. Tadamitsu Kishimoto, as Appendix A, providing the assurances requested by the examiner. Applicants have also amended the specification on page 3 to recite the date of deposit and the complete name and full address of the depository. In view of this declaration and amendment to the specification, it is requested that this rejection be withdrawn.

6. Rejections under 35 U.S.C. § 102

Claims 15, 16, 19, 24 and 25 are rejected as being anticipated by Suzuki *et al.*("Suzuki") as evidenced by Robbins and HarpersCollins Illustrated Medical Dictionary (1993) because the examiner broadly interprets the word "subject" as reading on Suzuki's treatment of human myeloma cell growth in mice with PM-1 antibody. Claim 15 is amended to recite the treatment of a human subject and that the disease treated is cachexia. Claims 16 and 19 directed treating plasmacytosis and hyperimmunoglobulinemia are cancelled. claims 24 and 25 depend from amended claim 15. It is believed that the amendment to claim 15 obviates the anticipation rejection over Suzuki and it is requested that this rejection be withdrawn.

7. Rejection under 35 U.S.C. § 103

Claims 15-28 are rejected as allegedly being obvious over Suzuki as evidenced by Robbins and HarpersCollins Illustrated Medical Dictionary (1993) as applied to claims 15, 16, 19, 24 and 25 and further in view of Sato *et al.*, Cancer Research, 53: 851-856 (1993) ("Sato"). The examiner bases this rejection on Sato's teaching of administering reshaped humanized PM-1 antibodies which bind to the IL-6 receptors to patients suffering from a disease caused by IL-6 production and Suzuki's disclosure that PM-1 and reshaped humanized PM-1 administered to SCID mice inhibit the growth of IL-6 dependent myeloma cells.

All of the claims are now limited to the treatment of cachexia, and therefore, the arguments will be limited to the applicability of the cited prior art against the amended claims. Applicants believe that the combination of Suzuki and Sato do not render obvious the claimed method of treatment of cachexia. Suzuki does not mention cachexia as one of the diseases associated with abnormal production of IL-6. Therefore, Suzuki does not provide a linking mechanism between the various disease and cachexia. The examiner argues that Robbins discloses that cancer causes a wasting syndrome referred to as cachexia and from this

observation, the examiner surmises that one skilled in the art would expect that a method which treats cancer would also ameliorate the symptoms of cancer, including cachexia. Applicants respectfully disagree with the examiner's rationale in this regard. In fact, applicants are not aware of any prior art which shows that an anti-IL-6R antibody inhibits the growth of cancer cells. Applicants believe that the anti-IL-6R antibody directly inhibits cachexia without the inhibition of cancer. The role of cancer is to induce cachexia but the inhibition of cachexia by anti-IL-6R antibodies does not mean that the anti-IL-6R antibody inhibits cancer. The examiner's rationale does not support her position of cause and effect.

Applicants enclose Souba *et al.* ("Souba") listed on the PTO-1449 and attached as Appendix B, to show the state of the art at the time of the priority date of the present invention. Souba discusses the relationship between cachexia and cytokines. According to Souba on page 589, line 2 to page 590, line 13, the only cytokine known to induce cachexia was tumor necrosis factor (TNF). Further, it was not known that the inhibition of IL-6 resulted in the inhibition of cachexia.

As stated by the examiner on page 6, section c. of the Office Action dated May 13, 1998, citing Durum, it was generally well known by a person with ordinary skill in the art that different cytokines exhibit similar actions, and therefore if a cytokine was inhibited another cytokine supplements the action of the inhibited cytokine. Therefore, it would not be expected that inhibition of IL-6 like action, and that inhibition of IL-6 alone results in inhibition of cachexia.

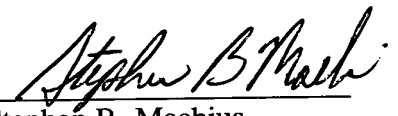
In regard, to the relationship of treating multiple myeloma and cachexia, applicants would like to direct the examiner's attention to Examples 2 and 3 of the present invention that show that anti-IL-6R antibody also inhibits cachexia induced by other types of cancer (i.e., colon 26 cancer and occ-1 cancer) than only multiple myeloma. This evidence shows that cachexia associated with cancers other than multiple myeloma can be treated by anti-IL-6R. The disclosures of Suzuki and Sato only tie the treatment of multiple myeloma cell growth in mice with PM-1 antibody. No other types of cancer are treated. These examples show that anti-IL-6R antibodies can be used to treat cachexia associated with other cancers than multiple myeloma.

In view of amendments to the claims and the above arguments, it is requested that this rejection be withdrawn.

Conclusion

In light of the foregoing amendments, remarks and enclosed appendices, applicants submit that all claims are in condition for allowance, and they solicit an early indication to that effect. Should the examiner believe that further discussion of any remaining issues would advance the prosecution, he is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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Date

Stephen B. Maebius
Reg. No. 35,264

FOLEY & LARDNER
Suite 500
3000 K Street, N.W.
Washington, DC 20007-5109
(202) 672-5300